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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/854,142	05/10/2001	Ilse Bartke	305J-900320US	6801

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QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.
P O BOX 458
ALAMEDA, CA 94501

EXAMINER	
HANLEY, SUSAN MARIE	
ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 04/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/854,142	BARTKE ET AL.	
	Examiner	Art Unit	
	Susan Hanley	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,12-15,17,19-23 and 25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,12-15,17,19-23 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants response filed 12/4/04 is acknowledged. Claims 1, 3-6, 12-15, 17, 19-23 and 25 are presented for examination.

Claim Rejections - 35 USC § 112

Claims 1 and 12 are rejected under 35 U.S.C. 1 12, first paragraph, because the specification, while being enabling for suppressing demyelination of the nerve fibers in the nervous system, does not reasonably provide enablement for prevention of the same. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant had previously amended claims 1 and 12 to recite "suppressing" the first line of each claim. However, the last line of each claim still recites "effective to prevent demyelination. The "preventing" language carries with it implication of totality of absence and possible occurrence thereof of the condition. There is neither explicit nor implicit teaching in Applicants specification or in the prior art where the totality and future occurrence of the condition of demyelination has been successfully prevented or eliminated. One of ordinary skill in the art or the person of skill in the art would be subjected to undue and laborious experimentation to determine the prevention of demyelination since Applicants' disclosure and the state of the art has no time tested standard for preventing demyelination. Since Applicants have used "suppressing," in other portions of the claims, it is respectfully suggested that the term "preventing" be replaced by "suppressing" in order to overcome this rejection.

Claims 1, 3-6 and 12 are rejected under 35 U.S.C., second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3-6 and 12 are rejected because the term "prevent" lacks antecedent basis in each claim.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 3-6, 12, 13, 17, 19-23 and 25 are rejected under 33 U.S.C. 103(a) as being unpatentable over Kramer et al. (1995) in view of Urschel et al. (1990), Althaus (WO 9303140), Unger et al. (EP 731,108) and Unger et al. (1995) and in further view of Weiner et al. (US 5,935,577).

Applicant argues that all of the requirements to establish a case of prima facie obviousness have not been met. Applicant asserts that the requirement for motivation to combine Kramer and either Urshcel/Althaues or Unger/Unger has not been established and at most is an invitation to experimentation. Applicant further asserts that the cited references do not provide a reasonable expectation of success to achieve the claimed invention because the references employ different specie models for demyelination. Applicant alleges that information derived from a rodent study may not be applicable to humans due to interspecies differences regarding receptors and the biological effects of growth factors. Applicant argues that the different references have different purposes: Althaus focuses on regenerating myelin, Unger/Unger focus on what concentrate of NGF will effect regeneration of myelin, while Urschel is concerned with showing that the removal of NGF affect myelination, and therefore provide no reasonable expectation of success. Applicant asserts that there is no reasonable expectation that rodent data (Kramer) can be combined with porcine data Unger/Unger. Applicant also alleges that the combination of references fails to teach all of the elements of the claims: "human or nonhuman primate," "suppressing demyelination in the optic nerve" or "interferon gamma."

The disclosures of Kramer et al. (1995), Urschel et al. (1990), Althaus (WO 9303140), Unger et al. (EP 731,108) and Unger et al. (1995) where discussed in the Office action of 2/9/04. It is further noted in Unger (EP 731,108) that there is a close relationship between regeneration and degeneration of myelin: "the identification and characterization of factors which are responsible for increased regeneration of OL

(oligodendrocytes) is very important for the molecular understanding of demyelinating diseases, such as multiple sclerosis and for the development of therapeutic agents" (col. 1, lines 15-23).

The combined references do not teach the relationship of model systems for demyelinating diseases.

Weiner et al. disclose "that experimental autoimmune encephalomyelitis (EAE) has been studies in mice and other rodent species as a model for immune therapies for MS. Those of ordinary skill in the art recognize that many of the potential immune therapies for MS are first tested in this animal model system" (col. 6, lines 45-55).

It would have been obvious to one of ordinary skill in the art at the time the invention was made that the results of NGF treatments of the various animal demyelination models would be a good indication of the efficacy of such treatments in humans or the closely related nonhuman primate. Weiner explicitly teaches that the various animal EAE models are regarded as a good approximation of the reaction that a human would have for taking NGF to suppress demyelination. Responding to Applicant's assertion that rat models may not provide a true picture for human or nonprimate reaction to NGF administration, Applicant does not provide any specific examples as to why the statement by Weiner et al. is invalid.

In response to applicant's arguments against the references individually, that is the assertion that there is no motivation to combine Kramer et al. with various combinations of the other references due to their differing area of research (demyelination vs. remyelination), one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The references (Kramer et al. (1995), Urschel et al. (1990), Althaus (WO 9303140), Unger et al. (EP 731,108) and Unger et al. (1995)) demonstrate the recognition that NGF can suppress demyelination and encourage remyelination. Unger (EP 731,108) taught that there is a close relationship between regeneration and degeneration of myelin. Therefore, Applicant argument that there is no motivation to

combine references due to their various foci is moot because demyelination and remyelination are closely related and the ordinary artisan would have expected that results in one area concomitantly provide relevant information for a related area of research. Thus, taken as a whole, the combined references are closely related and there is sufficient motivation to combine them to practice the instant inventions. Further, the ordinary artisan would have had a reasonable expectation that NGF would suppress demyelination in a human or nonhuman primate because the combined references are closely related and all demonstrate that the administration of NGF suppresses demyelination.

In response to Applicant's assertion that the references do not teach the claimed effect on interferon-gamma, the administration of NGF would naturally have this effect on a human or nonhuman primate that has ingested said NGF since it is a property of NGF. There is no requirement that a person of ordinary skill in the art would have recognized the claimed property of NGF at the time of invention, but only that the subject matter is in fact a natural property of NGF in the prior art reference. Schering Corp. v. Geneva Pharm. Inc., 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003).

Claims 14 and 15 are rejected under 33 U.S.C. 103(a) as being unpatentable over Kramer et al. (1995) in view of Urschel et al. (1990), Althaus (WO 9303140), Unger et al. (EP 731,108) and Unger et al. (1995) and in further view of Hammang et al. (US 5,904,144) and The Merck Manual (p. 1091).

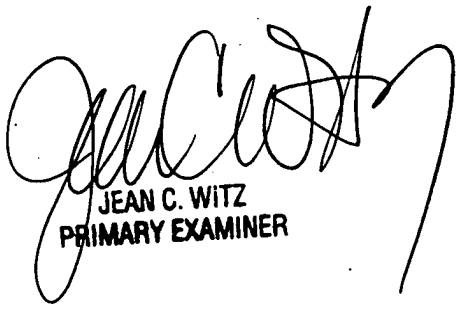
The disclosures of Kramer et al. (1995), Urschel et al. (1990), Althaus (WO 9303140), Unger et al. (EP 731,108) and Unger et al. (1995) where discussed in the Office action of 2/9/04. It is further noted in Unger (EP 731,108) that there is a close relationship between regeneration and degeneration of myelin: "the identification and characterization of factors which are responsible for increased regeneration of OL (oligodendrocytes) is very important for the molecular understanding of demyelinating diseases, such as multiple sclerosis and for the development of therapeutic agents" (col. 1, lines 15-23).

Hammang et al. teach methods for the delivery of a biologically active molecule to the eye via a surgically implanted capsule for diseases such as inflammatory optic neuropathies (col. 3, lines 63-68 to

col. 4, lines 1-4). NGF is a neurotrophic factor that can be transmitted to the optic nerve by the disclosed method (col. 4, lines 58). The disclosed methods are intended for a primate host such as a human, (col. 10, lines 65-68). Weiner et al. disclose that encapsulated NGF and a control were implanted into feline eyes. Post-explant NGF bioassay revealed that robust neurite outgrowth was seen for the eyes receiving NGF.

The Merck Manual teaches that optic neuromyelitis is the selective demyelination of the optic nerves and later the spinal cord (p. 1091, fifth paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to administer NGF to a patient having an inflammatory disease of the optic nerve. The ordinary artisan would have been motivated to do so because The Merck Manual teaches that inflammatory diseases are known to demyelinate the optic nerve. The cited prior art teaches that NGF is known to suppress demyelination and aid in remyelination of nerves in diseases such as MS. Further, Hammang et al. disclose that eye diseases such as optic neuromyelitis can be treated with neurotrophic factors such as NGF. The ordinary artisan would have had a reasonable expectation of success that NGF could be used to successfully treat optic inflammatory diseases because Hammang al. demonstrated that NGF can be administered to the optic nerve in amounts to induce neurite outgrowth, thus indicating that sufficient NGF can be administered to the optic nerve to suppress demyelination.



Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Susan Hanley
Patent Examiner
AU 1651